Aspects of Glucose Metabolism in Anoikis-induced Colorectal Cells

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Colorectal cancer (CRC) is the second most lethal cancer, and its survival rate drops from 90% to 14% when the condition is contained within the colon *vs.* when found at distant sites within the body. This is concerning because the disease will develop metastasis in 40-50% of patients. Metastasis is a multistep process in which cancer cells gain anoikis resistance to survive after detaching from primary locations and traveling through the circulatory and lymphatic systems to distant target organs. Thus, understanding the molecular drivers involved in glucose metabolism and its role in the anoikis process could be vital for improving the survival of CRC patients. Long non-coding RNA (lncRNA) is a class of RNA that does not directly code for protein but can hold many different roles in the cell. The lncRNA urothelial carcinoma-associated 1 (UCA1) aberrant expression has been identified in CRC and is associated with a poor prognosis. However, its function in glucose metabolism processes is not yet well defined. Our preliminary results in the anchorage-independent growth (anoikis) model demonstrate increased expression of lncRNA UCA1 and glucose uptake. Not only did the overexpression of lncRNA UCA1 lead to higher glucose consumption, but it also had an increased survival of anchorage-independent cells, which could indicate a potential mechanistic role of UCA1 in the modulation of glucose metabolism. Therefore, in this study, we propose elucidating the role(s) of UCA1 and its association with glucose metabolism during anoikis resistance. We hypothesize that the overexpression of lncRNA UCA1 enhances CRC metastasis by changing the glucose metabolism and, therefore, its anoikis resistance-associated pathways. We will utilize isogenic CRC cell lines SW480 (oncogenic) and SW620 (metastatic) to understand the mechanistic regulation of anoikis resistance. Stable overexpression (SW480+UCA1//GFP) and knockdown (SW620+ShUCA1) cell lines have been utilized for this study; both puromycin were selected and sorted. After subjecting these cell lines (along with the respective control) to anchorage-independent growth conditions, glucose pathway markers, pro-survival, anti-apoptotic, and stemness factors will be analyzed through RT-PCR, western blot, and Seahorse analyses. Utilizing the same model, we will examine lncRNA UCA1 linked anoikis resistance specific phosphorylation profiles of kinases and their protein substrates using the Proteome Profiler Phospho-Human Phospho-Kinase Array.